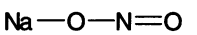
Sodium Nitrite

CAS #7632-00-0
Swiss CD-1 mice, at 0.0, 0.06, 0.12, and 0.24% in water
Robert Chapin, NTP/NIEHS Project Officer,
Dushyant Gulati, Leta Hommel Barnes,
Environmental Health Research and Testing
Started 5/19/88; Completed 12/4/90
NTIS #PB91132027



Sodium nitrite, a common food curing agent and an in vivo product of metabolic conversion of foodborne nitrates, was tested for its effects on reproduction and fertility in Swiss CD-1 mice using the RACB protocol. Data on food and water consumptions, body weights, and clinical signs from the dose-range-finding study (Task 1) were used to set exposure concentrations for the continuous cohabitation phase (Task 2) at 0.06, 0.12, and 0.24% weight per volume in drinking water. Water consumption was reduced by 10 to 17% in the 0.24% nitrite group, although F_0 body weights during Task 2 were not reduced. Data collected on body weight and water consumption allowed the calculation of estimated daily nitrite consumption as approximately 125, 260, and 425 mg/kg in the low, middle, and high dose groups, respectively.

Nine animals died during Task 2: three, four, zero, and one from the control through high dose groups, respectively. The variety of antemortem symptoms and the lack of a dose response suggest that these were not treatment related.

During Task 2, there was no treatment-related reduction of the mean number of litters per pair, the number of pups per litter, or the viability or weight of those pups. The cumulative days to deliver each litter was not affected.

The last litter from Task 2 was nursed by the dam until weaning. While mortality during nursing was not increased by nitrite exposure, pup body weights were reduced in the top dose group from postnatal day 7 to 21 by approximately 12 to 17%. In the accompanying table, "postnatal toxicity" is listed as unclear because although pup body weight gain was reduced, the pups were thrifty and mortality was not increased. One could speculate that this effect is due to reduced maternal water consumption, with consequent lower milk production.

Since no effects on reproduction were noted during Task 2, only the high dose and control mice were retained after weaning and examined in Task 4 for potential reproductive toxicity. Water consumption was measured several times during Task 4, and was found slightly reduced (by ≤8%). Body weights of F_1 mice were not different between groups at the beginning of the week of mating.

F_1 fertility and reproductive success during Task 4 was not affected by nitrite exposure: there was no change in the ability of the mice to mate or become pregnant or deliver live young. The number, weight, and viability of those young was not reduced by nitrite exposure.

After the delivery and analysis of the F_2 pups, the F_1 mice were killed and necropsied. Terminal body weights were not different between treated and exposed mice, and there were no treatment-related changes in any organ weight. The length and pattern of the estrous cycle was unchanged in the 12 days of evaluation, and the motility, concentration, and morphology of epididymal sperm was also unchanged by nitrite exposure. Histologically, the liver and kidneys of the 0.24% nitrite-treated and control mice were equivalent.

In summary, at concentrations that reduced water consumption slightly but did not reduce body weight, sodium nitrite had no adverse effect on reproductive performance or necropsy end points in Swiss CD-1 mice.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB91132027**
Chemical: **Sodium Nitrite**
CAS#: **7632-00-0**
Mode of exposure: **Water**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.06%	0.12%	0.24%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	—, —
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	•
Mortality	—, —	—, —	—, —
Feed consumption	•	•	•
Water consumption	—, —	—, —	↓, ↓
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F_1 generation — Dose concentration →	•	•	0.24%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	•	↓, ↓
Mortality	•	•	—, —
Adult body weight	•	•	—, —
Kidney weight[a]	•	•	—, —
Liver weight[a]	•	•	—, —
Feed consumption	•	•	•
Water consumption	•	•	↓, ↓
Clinical signs	•	•	—, —
Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•	•	—, —
Absolute testis, epididymis weight[a]	•	•	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	—

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	0.24%
NOAEL general toxicity:	0.12%
F_1 more sensitive than F_0?	No
Postnatal toxicity:	Unclear

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.